REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the above amendments and the following remarks. Claims 23-24, 29-36 and 41-46 are currently under consideration in the application. Following the above amendments, claims 29-34 and 41-46 have been canceled and claims 23-24 and 35-36 have been amended. Support for the above amendments can be found throughout the specification as originally filed and none of the amendments constitutes new matter. For example, support for the amendment to claim 23-24 and 35-36, reciting "nucleotide residues 1341-2694 of SEQ ID NO:110", can be found in Applicants' original disclosure of SEQ ID NO: 10 and 11, which contain sequences corresponding to nucleotide residues 1341-2105 and 2018-2694, respectively, of SEQ ID NO: 110. The above amendments, however, are not to be construed as acquiescence to the Examiner's grounds for rejection, and are made without prejudice to prosecution of any subject matter modified and/or removed by this amendment in a related divisional, continuation and/or continuation-in-part application.

Rejection Under 35 U.S.C. § 101

Claims 29-34 and 41-46 remain rejected under 35 U.S.C. § 101 as allegedly lacking specific, substantial and credible utility, or well established utility, for reasons already made of record. The Examiner also makes a related rejection to the same claims under 35 U.S.C. § 112, first paragraph, on the basis that because the claimed invention is not supported by a patentable utility, one skilled in the art would not know how to use the invention.

According to the Examiner, only claims having the subject matter of SEQ ID NO: 110 satisfy the utility requirements of 35 U.S.C. § 101, apparently in view of the previously submitted Declaration of Raymond Houghton, Ph.D., demonstrating the detection of SEQ ID NO: 110 in peripheral blood samples from prostate cancer patients. However, the Examiner maintains that SEQ ID NO: 110 is different from the claimed sequences of SEQ ID NO: 172-175, 177, 223 and 224 in that only SEQ ID NO: 110 has been detected as having a high level of expression in serum of patients with prostate cancer, as compared to normal healthy human. Thus the Examiner has maintained that absent a specific experimental showing that SEQ ID NOs: 172-175, 177, 223 and 224 are also detectable in, for example, blood samples from prostate

cancer patients, the claimed invention drawn to these SEQ ID NOs: lacks patentable utility under 35 U.S.C. § 101.

Applicants respectfully traverse this rejection on the basis that it is not necessary, in order to satisfy the utility requirements of 35 U.S.C. § 101, to demonstrate experimentally that SEQ ID NOs: 172-175, 177, 223 and 224 can be detected in blood samples from prostate cancer patients, when the skilled artisan, in view of Applicants' disclosure, and in view of the general level of knowledge in this art, would fully recognize a reasonable likelihood of success in practicing such methods.

In this respect, it is submitted that the Examiner has applied against Applicants a standard for patentable utility that exceeds the requirements proscribed by 35 U.S.C. § 101. An applicant is not required to provide evidence sufficient to establish that an asserted utility is true "beyond a reasonable doubt." *In re Irons*, 340 F.2d 974, 978, 144 USPQ 351, 354 (CCPA 1965; emphasis added); *See also* MPEP 2107.02. Moreover, an applicant need not provide evidence that establishes an asserted utility "as a matter of statistical certainty." Rather, a rigorous correlation is not necessary when a test is reasonably predictive of a result. *Nelson v. Bowler*, 626 F.2d 853, 856-57, 206 USPQ 881, 883-84 (CCPA 1980; emphasis added). Further still, in order to overcome the presumption of truth that an assertion of utility by the Applicant enjoys, Office personnel must establish that it is more likely than not that one of ordinary skill in the art would doubt (*i.e.*, "question") the truth of the statement of utility." (*e.g.*, MPEP 2107.02 IIIA; emphasis added).

Applicants maintain that the skilled artisan would more likely than not concur that the Applicants' claimed sequences, based upon their identified prostate-specific expression profiles, indeed possess utility under 35 U.S.C. § 101 in the context of the claimed invention, irrespective of whether Applicants have presented experimental confirmation for each and every sequence claimed.

Moreover, if the proper legal standard sufficient for establishing utility under 35 U.S.C. § 101 is applied against the instant claims, the disclosures of Kibel *et al.* and Ren *et al.*, taken either individually, or in combination, do not negate the skilled artisan's recognition that Applicants' asserted utilities are more likely than not true. Applicants certainly acknowledge

that, in some instances, a protein may have altered expression in metastatic cancer versus primary cancer, as suggested by the Examiner. This does not, however, compromise the general contention set forth by Applicants that there would be a reasonable expectation that the prostate-specific sequences currently claimed are useful in the detection of prostate cancer in a patient.

Therefore, collectively, in view of Applicants' specification as originally filed, in view of the previously submitted Declaration of Raymond Houghton, Ph.D., and further in view of the level of general knowledge in this art, Applicants submit that the skilled artisan would expect that the presently claimed invention possesses patentable utility under 35 U.S.C. § 101.

Nevertheless, in the interest of advancing prosecution of the subject application, and without acquiescing to the stated grounds for rejection, Applicants have canceled claims 29-34 and 41-46, thereby rendering moot the Examiner's rejection under 35 U.S.C. § 101, and the related rejection under 35 U.S.C. § 112. These amendments, however, are made without prejudice to prosecution of the same or similar subject matter in a related application.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 35-36 and 41-46 stand rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification allegedly does not contain a written description of the invention in sufficient detail that one skilled in the art can reasonably conclude that Applicants had possession of the claimed invention at the time of filing. More particularly, the Examiner asserts that the specification fails to identify and describe the 5' and 3' regulatory regions and untranslated regions allegedly essential to the function of the claimed invention, which, according to the Examiner, are required because the claimed invention currently encompasses genes.

Applicants respectfully traverse this rejection and submit that the 5' and 3' regulatory and untranslated regions are not essential to the function of the claimed invention since the invention is drawn to detecting the presence of expressed polynucleotide sequences of the recited SEQ ID NOs. For purposes of clarity and to advance prosecution, Applicants have canceled claims 41-46 and have amended claim 35, without prejudice or acquiescence, to specify that the sequences being detected according to the claimed methods are "expressed" polynucleotide sequences. Reconsideration of this rejection is thus respectfully requested.

Claims 35-36 also stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to reasonably provide enablement for a method of detecting the presence of a DNA molecule of SEQ ID NO: 110 in any and all biological sample. The Examiner acknowledges that the specification is enabling for a method of detecting the presence of a DNA molecule of SEQ ID NO: 110 in a blood sample. However, according to the Examiner, it is unpredictable whether prostate cancer cells that have metastasized to non-prostate tissues would retain expression of the claimed sequence because expression of such a sequence could be lost during progression toward metastasis.

Applicants respectfully traverse this rejection and submit that the skilled artisan, in view of the specification as originally filed, and further in view of the previously submitted Declaration of Raymond Houghton, Ph.D., would reasonably expect that the claimed method could be used to detect distant metastases in non-prostate tissues according to the claimed invention. The skilled artisan would further expect that expression of the claimed sequence would be retained in these distant metastases, particularly given that expression of the claimed sequence was demonstrated by Applicants to be retained and detectable in circulating prostate cancer cells in the sera of prostate cancer patients.

However, again, in the interest of advancing prosecution of the subject application, and without acquiescing to the stated grounds for rejection, Applicants have canceled claims 41-46 and have amended claim 35 such that the biological sample used according to the claimed methods is selected from the group consisting of blood and semen, as recited in claim 23. Reconsideration of this rejection is respectfully requested.

Rejection Under 35 U.S.C. § 102

Claims 23-24 and 35-36 stand rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent No. 6,130,043. According to the Examiner, U.S. Patent No. 6,130,043 teaches a method for detecting prostate disease employing polynucleotides (SEQ ID NOs: 15 or 16) having a high degree of structural similarity to Applicants' claimed SEQ ID NO: 110. The Examiner concludes that because the method of the prior art comprises the same method steps as claimed in the instant invention, the claimed method is anticipated because the method will inherently lead to the claimed effects.

Applicants respectfully traverse this rejection. The instant specification discloses that the sequence referred to as L1-12 was originally isolated from a prostate tumor specific library as two separate clones, SEQ ID NOs: 10 and 11 (*e.g.*, page 25, lines 3-7), the full length cDNA sequence of which was subsequently identified as SEQ ID NO: 110 (*e.g.*, page 25, lines 26-28). Applicants have amended claims 23-24 and 35-36 such the at least two oligonucleotide primers employed in the claimed methods are specific for a DNA molecule corresponding to nucleotide residues 1341-2694 of the polynucleotide sequence of SEQ ID NO:110. Applicants note that SEQ ID NOs: 10 and 11 were first filed by Applicants in priority Application Serial No. 08/806,596, filed February 25, 1997. Applicants further note that SEQ ID NOs: 10 and 11 represent overlapping cDNA sequences corresponding to nucleotide residues 1341-2105 and 2018-2694, respectively, of SEQ ID NO: 110. Accordingly, the above amendment now requiring that the oligonucleotide primers used in the claimed methods be specific for nucleotide residues 1341-2694 of SEQ ID NO:110 effectively removes the prior art cited by the Examiner under 35 U.S.C. § 102(e), as the subject matter of the amended claims, first disclosed February 25, 1997, clearly pre-dates the earliest claim to priority of U.S. Patent Nos. 6,130,043. Reconsideration and withdrawal of this rejection under 35 U.S.C. § 102(e) is thus respectfully requested.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

All of the claims remaining in the application are now clearly allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

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